Estrogenicity of Environmental PCBs

The paper by Bergeron, Crews, and McLachlan, "PCBs as Environmental Estrogens: Turtle Sex Determination as a Biomarker of Environmental Contamination" (*EHP* 102:780–781) presents data on the estrogenic activity of 11 chlorinated biphenyls or diphenyl ethers, or hydroxylated derivatives thereof, selected so as to represent a variety of structural types. Some of the PCB types examined (e.g., compounds A, C, D, E, and J) arise from PCB congeners actually detectable in the commercial Aroclors (*1*) and hence also in environmental samples, whereas other PCB types (e.g., those with heavily uneven chlorination of the two rings, as in compounds F,G, and L) arise from PCB congeners that are not detectable in either the Aroclors themselves (*1*) or even environmentally transformed PCB compositions (*2*). It is noteworthy that the only compounds found to have statistically significant estrogenic activity (compounds F and G) both represented 4-hydroxylation products of PCB congeners belonging to the nonenvironmental group, whereas the five compounds representative of PCB structures actually present in the environment were all negative. In short, the results present zero evidence that environmental PCBs present risk of estrogenic activity.

This is hardly what the authors claim, however. In their discussion they state (p. 781):

> This report contributes laboratory evidence of the effect of PCBs on sex determination . . . and serve as a warning of conditions threatening wildlife populations. The PCB levels reported here as effective in disrupting normal gonadal differentiation in the turtles are comparable to average levels of PCBs found in human breast milk in industrialized nations.

This most misleading statement represents a false alarm that can only impede the search for the environmental contaminants that actually do present estrogenic risk.

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References

1. Shulz DE, Patrick G, Duinker JC. Complete characterization of polychlorinated biphenyl congeners in commercial Aroclor and Clophen mixtures by multidimensional gas chromatography-electron capture detection. Environ Sci Technol 23:852–859 (1989).
2. Brown JF Jr, Wagner RE. PCB movement, dechlorination and detoxication in the Acushnet estuary. Environ Toxicol Chem 9:1215–1233 (1990).

Response to Hamilton

There are several points we would like to address in our response. First of all, the compounds studied were chosen because these particular congeners were believed to be estrogenic based on their conformational structure. The primary reason for conducting this type of study was to show the effectiveness of a temperature-dependent sex determined (TSD) species as a tool in assessing estrogenic activity *in vivo*. This point is furthered by an earlier report in *EHP* by Guillette et al. (*1*). While the PCB compounds we used may not be primary components of commerically available PCB mixtures, there are parallels between these compounds and other PCB congeners in the pattern of *ortho*-chlorine substitutions, as Korach et al. (*2*) indicate. It is important to study how these structures affect a developing organism in order to understand how PCBs can act as estrogens. Though these particular congeners may not be currently used in the readily available mixtures, McKinney et al. (*3*) make reference to goals of using PCBs that are easily detoxified via hydroxylation. If such considerations lead to composition of commercially available PCB mixtures away from congeners that exhibit a dioxinlike toxicity, these considerations should include assessment of the estrogenic activity of these compounds. The TSD system can be used to test such mixtures *in vivo*. Furthermore, the appearance of hydroxylated PCB congeners in "nature" is an emerging issue: for example, Bergman et al. (*4*) report that the hydroxylated forms of heavily chlorinated (penta- or heptachlorinated) biphenyls were among the most retentive forms of PCBs found in blood from humans or seals. Clearly, this class of molecules may have environmental significance which is only now being appreciated.

The second point that we would like to emphasize regards the potential for second-generation exposure to PCBs as environmental estrogens. While the congeners that we found to clearly exhibit estrogenic activity may not be produced in the commercial PCB mixtures, or even found in soil and water samples, they may exist within animal tissue during metabolism of the environmental compounds. Maternal metabolic by-products may affect the reproductive system at a critical stage in development of the offspring, producing the detrimental estrogenic effect on the second generation. This is particularly a concern when enhanced estrogenic effects are produced by the synergy of different combinations of low-level PCBs, an issue brought to light by the study in question.

Finally, we share Dr. Hamilton's concern that false alarms may impede identification of contaminants that actually present risk of estrogenic activity. However, Dr. Hamilton's cited quotation of our discussion, and his interpretation of it, require clarification so as not to be misleading. Dr. Hamilton's abbreviated quote would lead readers to believe that it is our report which we say serves as a warning of threatening environmental conditions. In fact, the passage he omitted clearly identifies "the usefulness of a TSD species as a biomarker" to serve in the capacity which Dr. Hamilton apparently ascribes to our report.

Our findings support the call from the scientific community for the need to further study the mechanisms of estrogenic activity of environmental contaminants. These findings, together with the growing body of evidence that a number of environmental compounds mimic estrogens and do have an effect on developing reproductive systems, provide ample indication for further investigation of these mechanisms and their outcomes. Our report suggests a model by which to continue these efforts, and we appreciate the continued interest in our work and the opportunity to address questions regarding it.

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References

1. Guillette LJ Jr, Gross TS, Masson GR, Matter JM, Percival HF, Woodward AR. Developmental abnormalities of the gonad and abnormal sex hormone concentrations in juvenile alligators from contaminated and control lakes in Florida. Environ Health Perspect 102:680–688 (1994).
2. Korach KS, Sarver P, Chae K, McLachlan JA, McKinney JC. Estrogen receptor-binding activity of polychlorinated hydroxybiphenyls: